REMARKS

Claims 1 and 3-34 are pending in the application. Claim 2 is cancelled. Claims 5-23 and 25-34 are withdrawn. Claims 1, 3, and 24 have been amended. Claims 1, 3, 4 and 24 are currently under examination.

The specification has been amended to remove all reference to claim numbers and correct minor grammatical errors. The informalities noted by the examiner have been corrected. No new matter has been added.

Rejections under 35 U.S. § 112 first paragraph

According to the Examiner, "the specification does not reasonably provide enablement for a null mutant non-human animal characterized in showing salt intake behavior similar to that of wild-type animals under water-sufficient conditions and showing much more intakes of hypertonic saline compared with wild-type animals under water and salt depleted conditions and methods of using same." Therefore, the Examiner is of the opinion that the specification does not enable a person of skill the art to make or use the invention commensurate in scope with these claims.

Citing Mullins *et al.* (Journal of Clinical Investigation, 1996), the Examiner asserts that ES cells are only available for mice. However, in its final sentence, Mullins *et al.* states:

> "Despite the lack of germline transmission to date, major efforts continue to be toward the generation and use of ES cells from nonmurine species, using both traditional and new technologies, and the availability of such cells is likely to accelerate both the use of such species and the precision with which genetic changes can be introduced." (p. S39)

As is clear from the above citation, germ transmission is not an essential component in producing an animal model using murine other including mouse, but rather the direction of research in the technical field is directed to produce such ES cells. Therefore, it is respectfully submitted that one cannot conclude that ES cells are not available in the species other than mouse.

The Examiner further states on page 9 of the Office Action that the invention of the present application is not enabled because the results of gene targeting at a particular loci are unpredictable. Specifically, the Examiner states,

> "The enabled scope of the claimed invention is also based on the unpredictable state of the transgenic knockout art in that disruption of a different exon of the same gene may **not** result in the anticipated phenotype. See Moreadith et al. (Journal of Molecular Medicine, 1997) who support phenotypic unpredictability in knockout mice. In particular, Moreadith et al. discuss that gene targeting at a particular loci is unpredictable with respect to the resulting phenotype since often the generation of knockout mice, in many instances, changes the prevailing notions regarding the functions of the encoded proteins. For example, Moreadith et al. report that gene targeting at the endothelin loci led to the creation of mice with Hirschsprung's disease instead of the anticipated phenotype (abnormal control of blood pressure). See page 208, column 2, 2nd paragraph."

It is respectfully submitted that the Examiner's position is not in accordance with an assumption widely shared by the people skilled in the genetic engineering art. Persons skilled in the art are not only working on the study of the correspondence in mice between disrupted genes and phenotypes. It is clear that the significance and goal of the genetic engineering art is to elucidate the genetic characteristics of humans by investigating as a representative the genetic characteristics of mice, which are readily available and easily engineered. In fact, it is rather a common assumption that a genetic characteristic newly found in mice applies to animals other than mice.

Further, if the enablement and description requirements are satisfied only based on the examples regarding particular sites of particular genes that are disclosed in the specification, only part of the novel technical idea that has industrial applicability is granted as patent. Applicants urge that they are entitled to the full breadth and scope of the claimed invention in accordance with the intention and spirit of the U.S. Patent law.

Relating to the scope of claim, there are patent documents found in the "Patent Full-Text and Full-Page Image Databases" at the USPTO, claiming "non-human animal" or "non-human mammal" but disclosing examples using mice only.

For example, US 5,880,327 claims "non-human mammal" (claim 1) and limits the "non-human mammal" to mouse, rat, rabbit, pig, sheep, goat and cattle (claim 10). However, US 5,880,327 only discloses examples using mice (Example 2). Therefore, it is evident from US 5,880,327 that a wide scope of claim such as the one relating to "non-human mammal" can be allowed in the US practice even if there are only limited examples using mice.

Further, US 5,849,997 claims "non-human mammal" (claim 1). However, the Example in the specification discloses the cases using mice. Therefore, it is also evident from US 5,849,997 that a wide scope of claim such as the one relating to "non-human mammal" can be allowed in the US practice even if there are only limited examples using mice.

Still further, US5,831,141 claims "non-human mammal" (claim 1). However, the Example in the specification discloses the cases using mice and pig. Regarding to other species of animals, it only states "[m]ethods for microinjection of other animal species are similar to the methods set forth above" (Example 3 (3) Other Animals). Therefore, it is also evident from US 5,831,141 that a wide scope of claim such as the one relating to "non-human mammal" can be allowed in the US practice even if there are only limited examples using mice and pig.

In light of the above arguments, reconsideration and withdrawal of the rejection are respectfully requested.

Rejections Under 35 USC § 112 second paragraph

1. With respect to claim 1, the Examiner states that,

> "The term "much more" in claim 1 is a relative term which renders the claim indefinite. The term "much more" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of

ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear how much intake of hypertonic saline would be considered "much more". Appropriate correction is requested.

Claim 1 has been amended to eliminate the term "much more." Accordingly, it is respectfully submitted that the claim is free of indefiniteness rejections.

2. With respect to claim 2, the Examiner states:

"Claim 2, as written, is unclear. The claim recites that the in the null mutant animal, the function of the Nav2 gene is deficient on "its chromosome". It is unclear what "its chromosome" refers to – the animal's chromosome (in which case, it would be expected that the animal would have more than one chromosome. or the chromosome on which the Nav2 gene is found. Appropriate correction is required. Claims 2-3 and 4 depend from claim 4."

Claim 2 has been cancelled, thereby obviating the rejection.

3. Claim 3 has been amended to depend from claim 1. It is respectfully submitted that because claim 1 is now in an allowable form, claim 3 is also allowable.

Claim 24

4. Claim 24. According to the Examiner:

"Claim 24, as written, is unclear. The claim is drawn to a method of screening a material that promotes or suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level characterized in using the non-human animal according to claim 1, and a subject material. However, no clear and defined steps are recited in the independent claims. While minute details are not requested in method claims, at least the basic steps must be recited in a positive, active fashion. See Ex Parte Erlich, 3 USPQ2d, p. 1011 (Bd. Pat. App. Int. 1986).

Applicants respectfully direct the Examiner's attention to the paragraph on pages 18-19 of the specification which states:

"Concrete examples of a screening method with the null mutant non-human animals showing salt intake behavior similar to that of the wild-type animals under water-sufficient conditions and showing much more intakes of hypertonic saline compared with the wild-type animals under water- and salt-depleted conditions or the transgenic non-human animals which excessively express a gene that codes for a protein acting as a sensor of extracellular sodium ion level and the subject material include; a method wherein nerve cells obtained from the null mutant non-human animals showing salt intake behavior similar to that of the wild-type animals under water-sufficient conditions and showing much more intakes of hypertonic saline compared with the wild-type animals under water- and salt-depleted conditions, or from the transgenic non-human animals which excessively express a gene that codes for a protein acting as a sensor of extracellular sodium ion level are brought into contact with a subject material *in vitro*, and then the change of the function or the expression of said protein is measured/evaluated; a method wherein saline is administrated to said null mutant non-human animals or to said transgenic non-human animals beforehand, then the nerve cells obtained from said non-human animals are cultured in the presence of the subject material, and the change of the function or the expression of said protein is measured/evaluated; a method wherein saline and a subject material are administrated to said null mutant non-human animals or to said transgenic non-human animals beforehand, then the change of the function or the expression of said protein in the nerve cells obtained from said non-human animals is measured/evaluated; a method wherein saline and a subject material are administrated to said null mutant non-human animals or to the transgenic non-human animals beforehand, then the change of the function or the expression of said protein in the non-human animals is measured/evaluated."

From the above citation, it is evident that the steps of claim 24 are clear. Claim 24 is characterized by an essential matter, and therefore, the claim is not indefinite. Additionally, claim 24 is amended to replace the term "subject material" with "transgenic non-human animal which excessively expresses a protein acting as a sensor of extracellular sodium ion level." If the claim is still considered to be indefinite, the Examiner's suggestions for acceptable language would be welcome.

In light of the amendments and arguments presented, it is believed that the application is in condition for allowance, and notice to that effect is respectfully requested.

Respectfully submitted,

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